Emergence of Multidrug-resistant *Salmonella* Newport, United States

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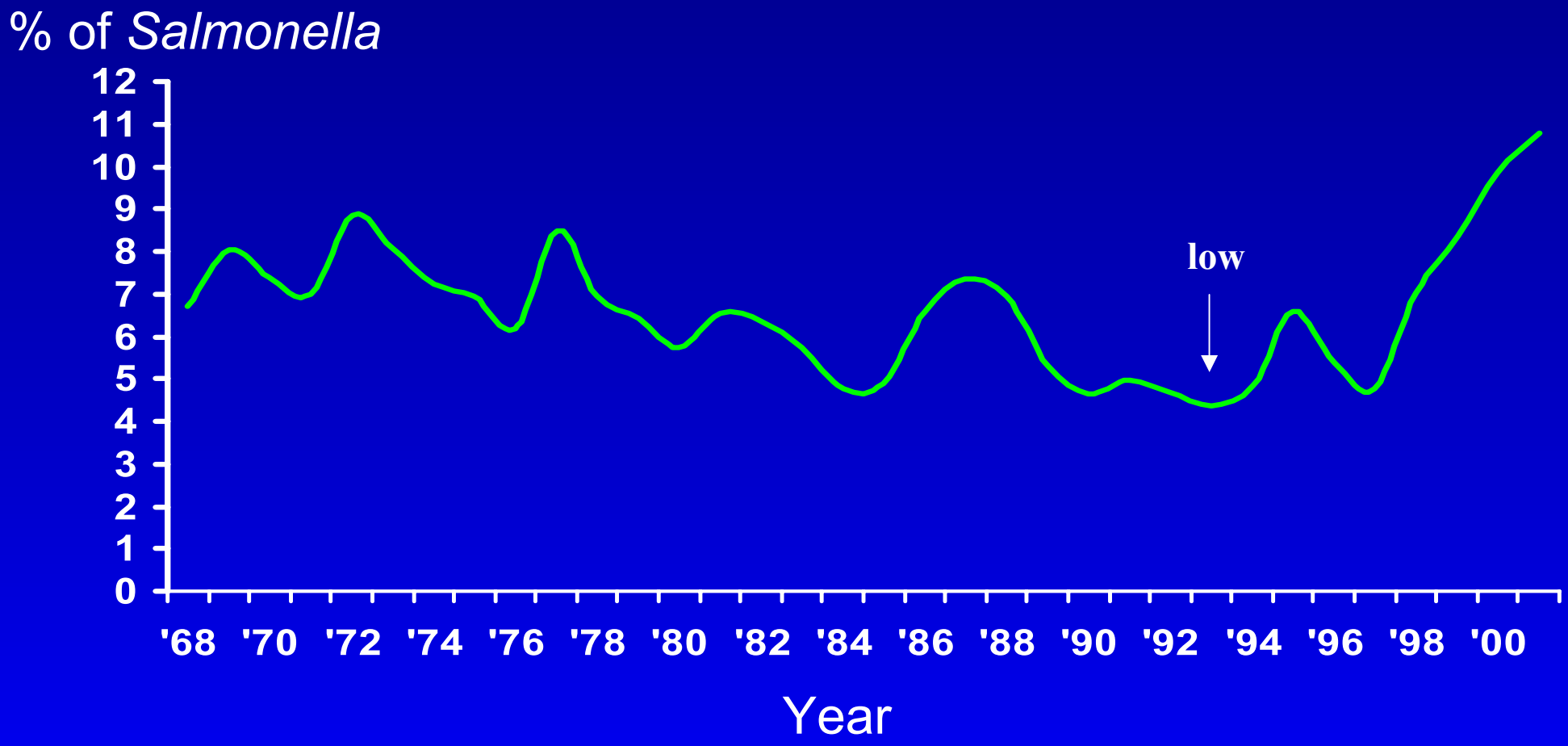
CSTE Annual Meeting, June 2002

Salmonella in the U.S.

- Estimated annual burden
  - 1.4 million cases
  - 600 deaths
- State laboratories confirm and serotype
  - ~33,000 isolates/year
  - Represent ~2.4% of total estimated cases
  - Provide critical information for detecting emerging pathogens

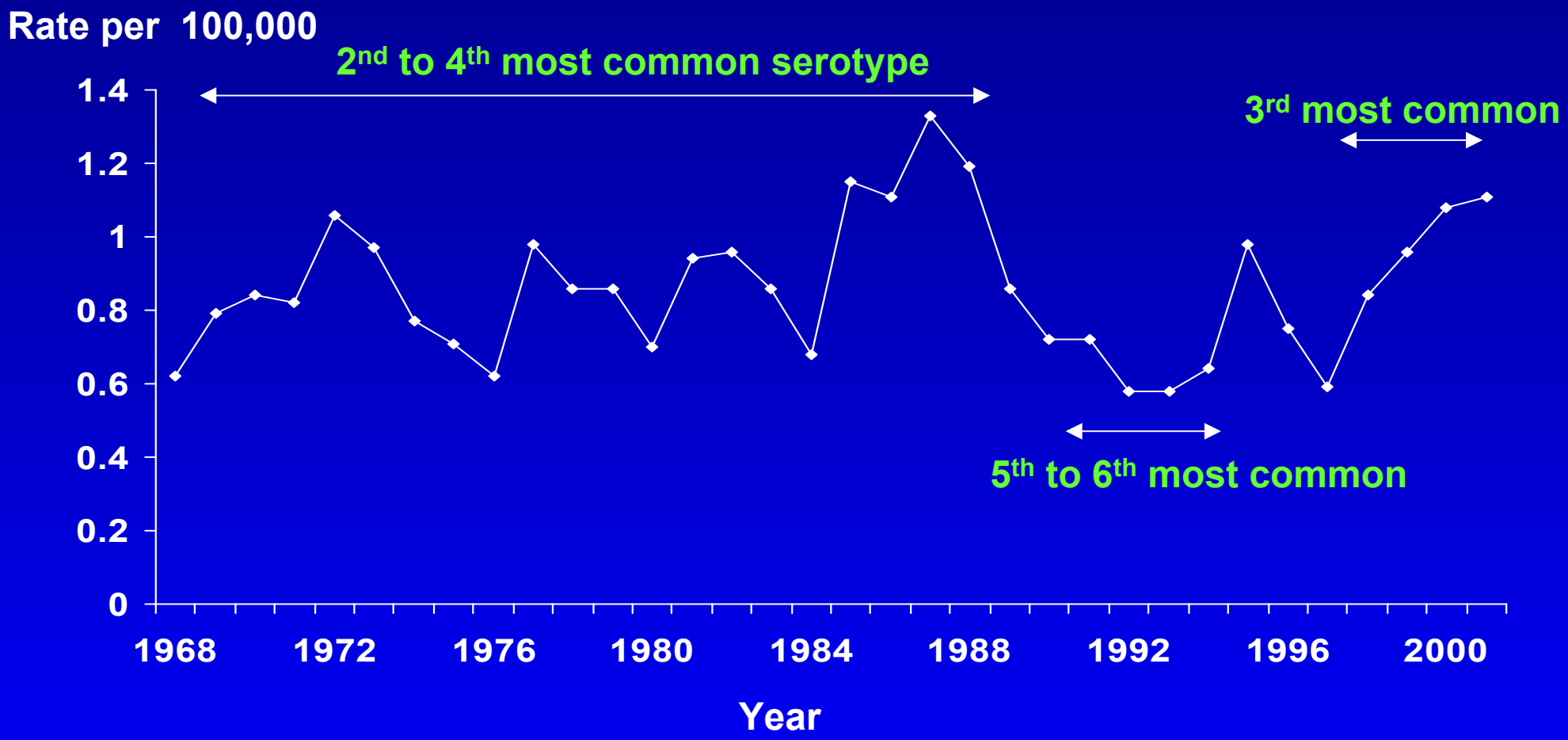
Mead et al, EID, 1999
CDC Public Health Laboratory Information System (PHLIS)

Proportion of serotyped *Salmonella* that were *S.* Newport, 1968 to 2001



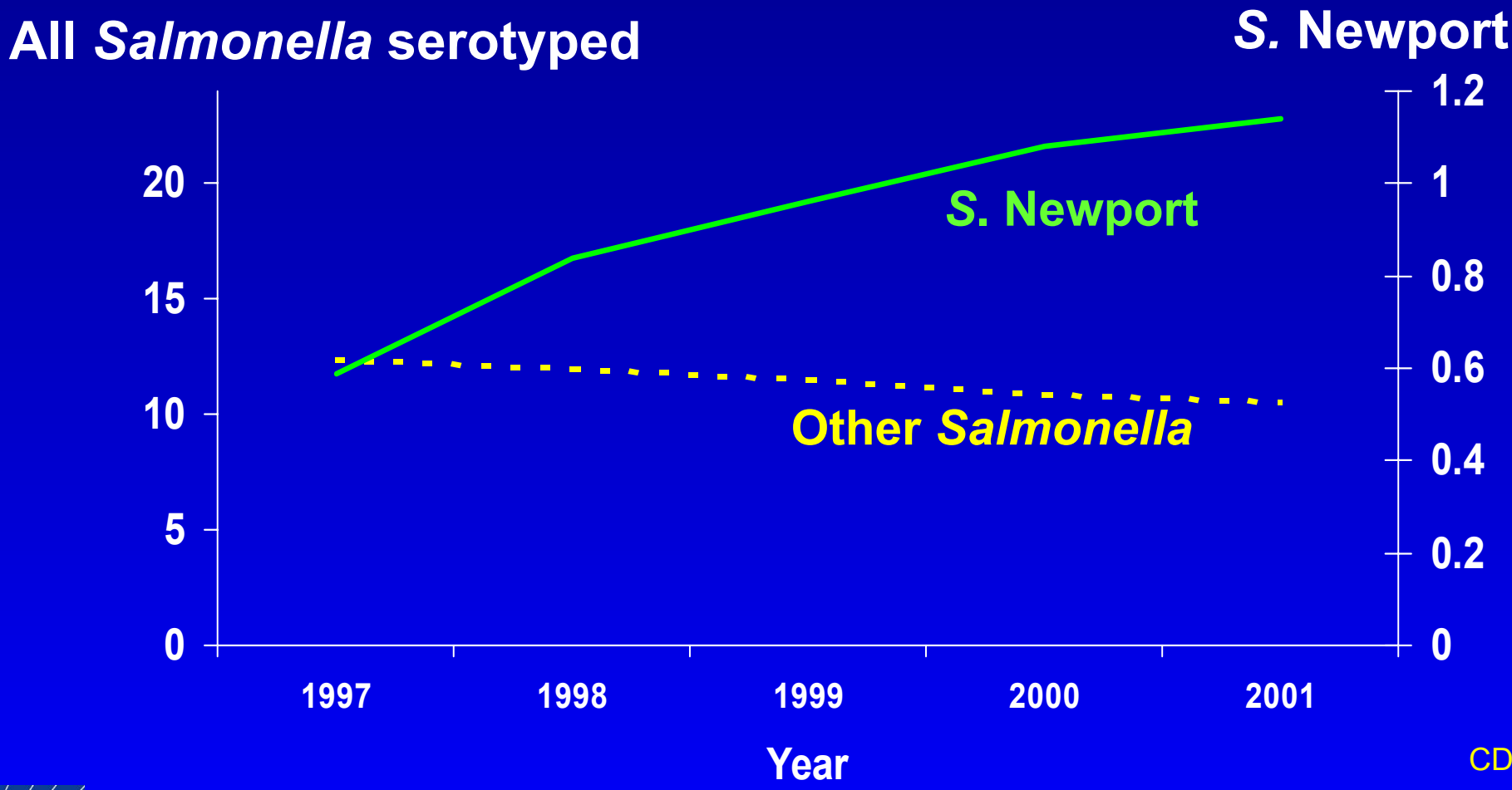
CDC PHLIS

Incidence of human *S.* Newport Isolations, United States, 1968-2001



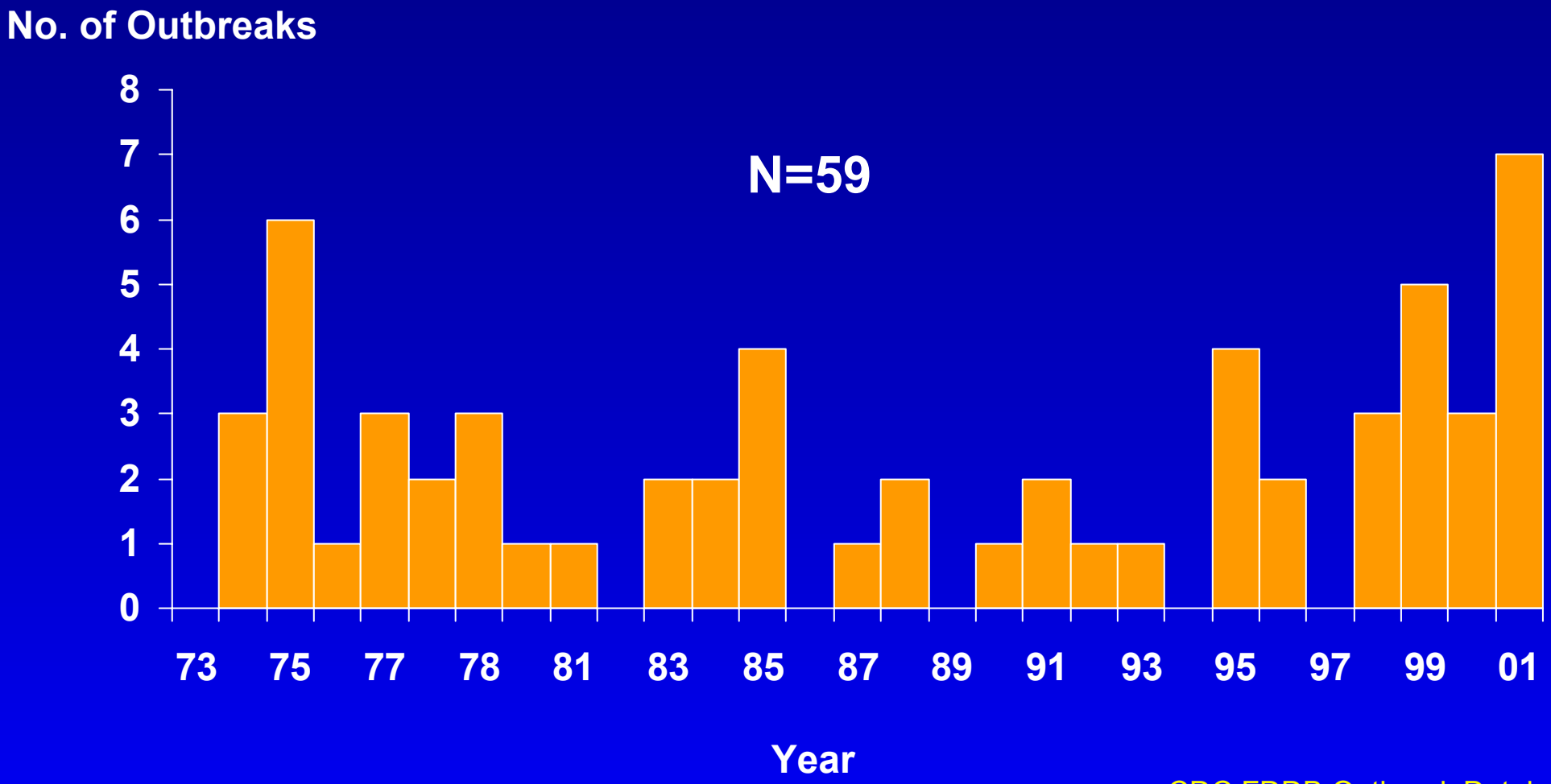
CDC PHLIS

Incidence of *S.* Newport compared with other serotyped *Salmonella*, 1997-2001



CDC PHLIS

Foodborne Outbreaks of *S.* Newport, 1973-2001

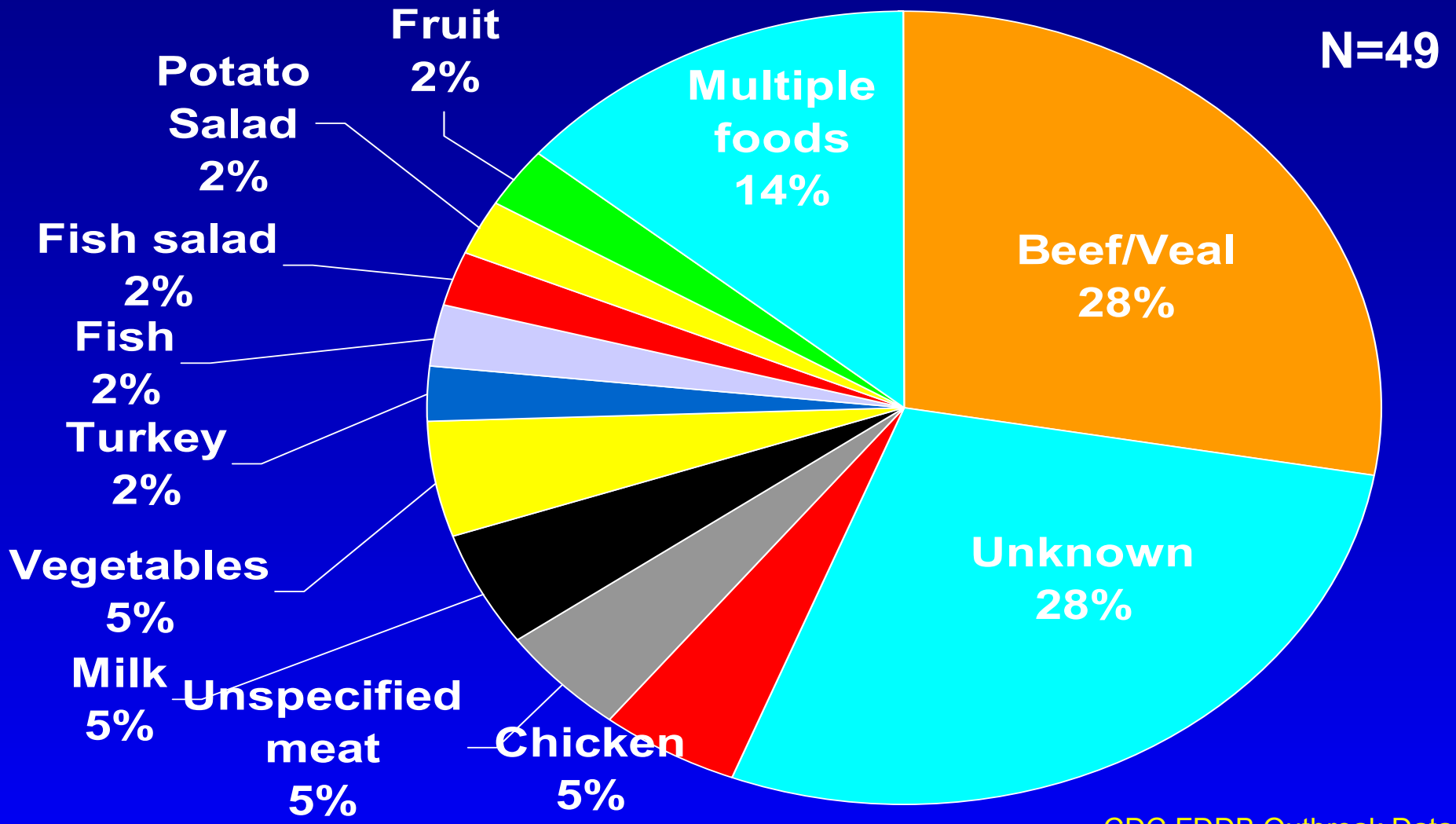


CDC FDDB Outbreak Database
2000-2001 provisional data

Increase in *S.* Newport

- What food items are historically associated with *S.* Newport infections?
- What factors may be associated with the increased incidence?

Vehicles Implicated in *S. Newport* Foodborne Outbreaks, 1973-1999



CDC FDDB Outbreak Data

Selected *S.* Newport outbreaks, 1973-1995

Year	State	Vehicle	Resistance	Reference
’73	CO	Ground beef	SSuT	Fontaine AJE
’83	MN	Ground beef	AT	Holmberg NEJM
’85	CA	Ground beef	ACSSuT	Spika NEJM
’95	CA	Alfalfa sprouts	none	Van Beneden JAMA

Resistance to ACSSuT

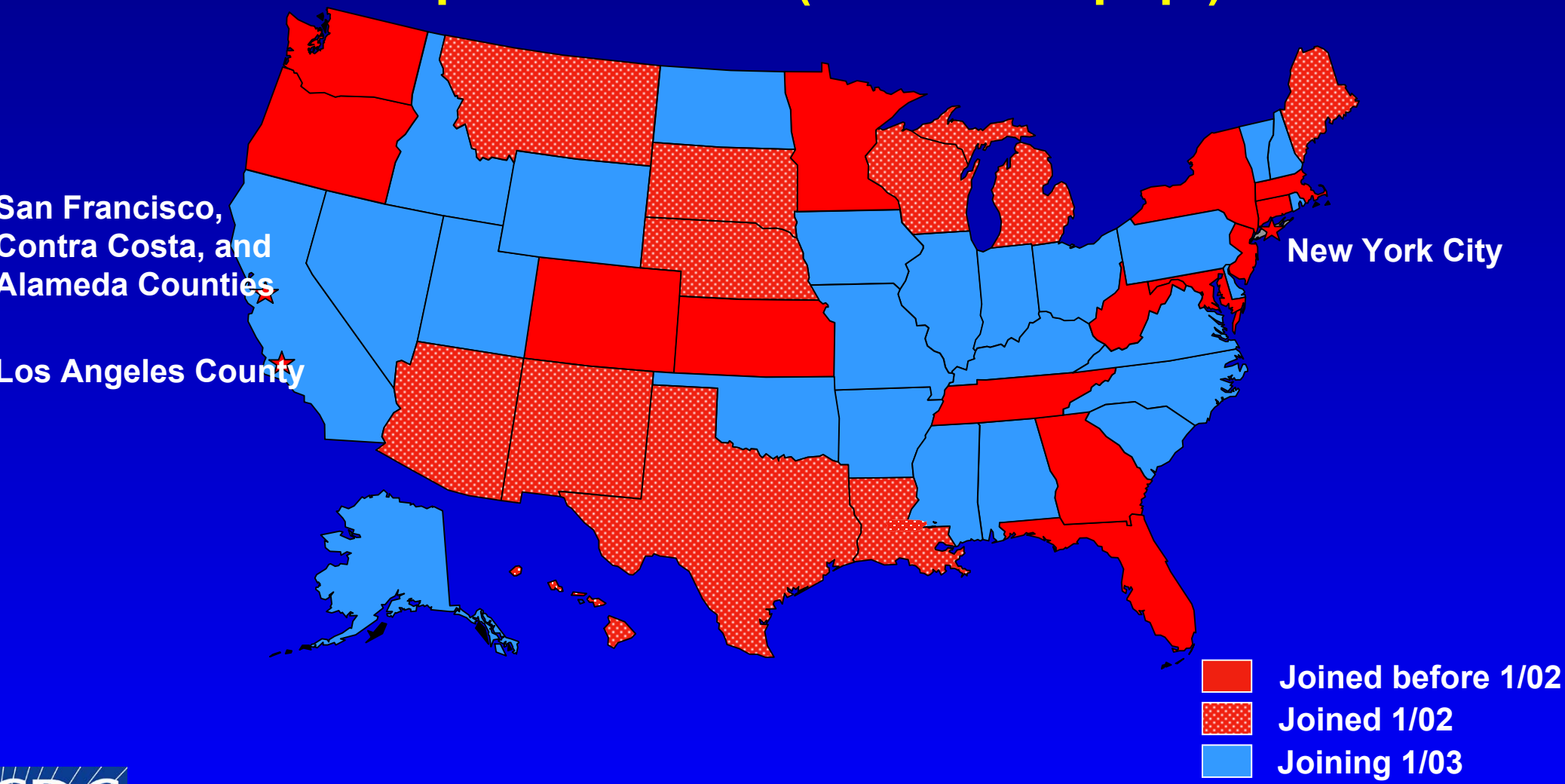
- Resistance to:
  - Ampicillin (A)
  - Chloramphenicol (C)
  - Streptomycin (S)
  - Sulfamethoxazole (Su)
  - Tetracycline (T)

Antibiotic treatment of *Salmonella* infection

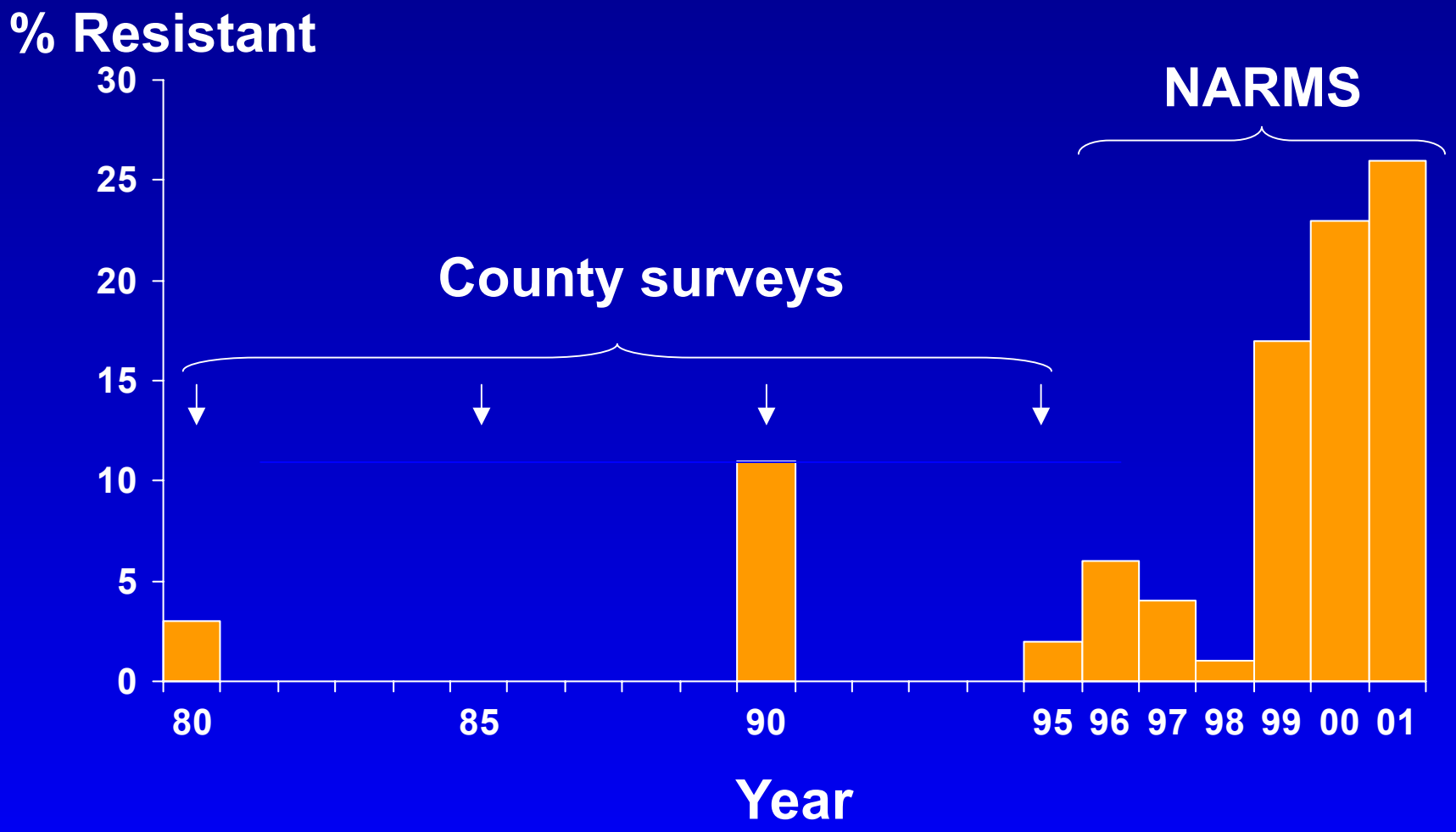
- Not needed for mild diarrhea
- Used to prevent complications in neonates, immunosuppressed, persons >50 years old
- Life-saving in invasive infections (e.g., meningitis)
- Important agents are amoxicillin, ceftriaxone, ciprofloxacin, trimethoprim-sulfa

National Antimicrobial Resistance Monitoring System (NARMS)

Pop. 158 million (56% of US pop.)



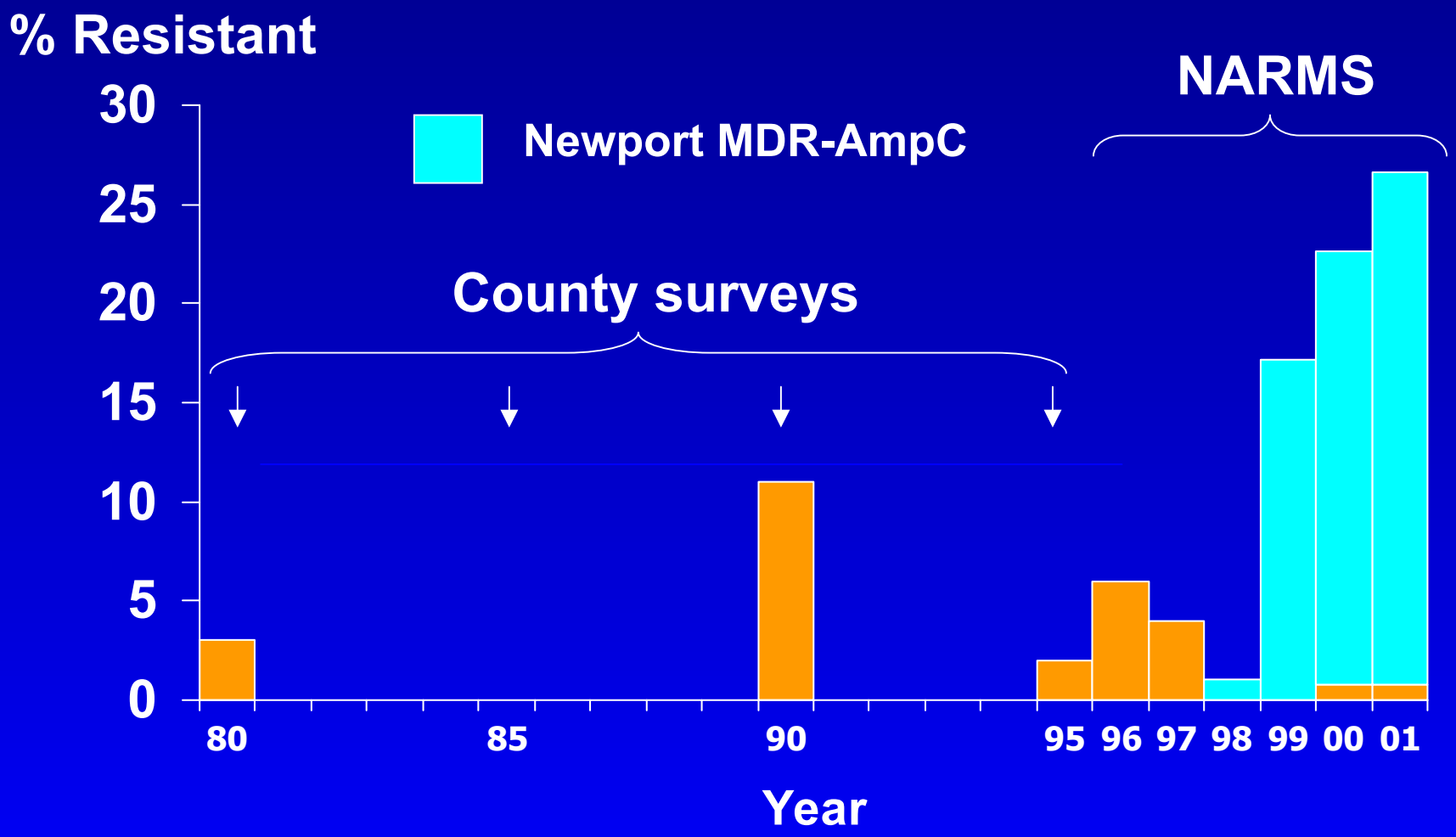
Proportion of human *S.* Newport resistant to at least ACSSuT



"Newport MDR-AmpC" A new resistance pattern

- *S.* Newport resistant to ACSSuT plus
  - Amoxicillin-clavulinic acid (penicillin-inhibitor combination)
  - Cephalothin (1st generation cephalosporin)
  - Cefoxitin (cephamycin)
  - Ceftiofur (veterinary agent) and intermediate or resistant to ceftriaxone (extended-spectrum cephalosporins)

Proportion of human *S.* Newport resistant to at least ACSSuT



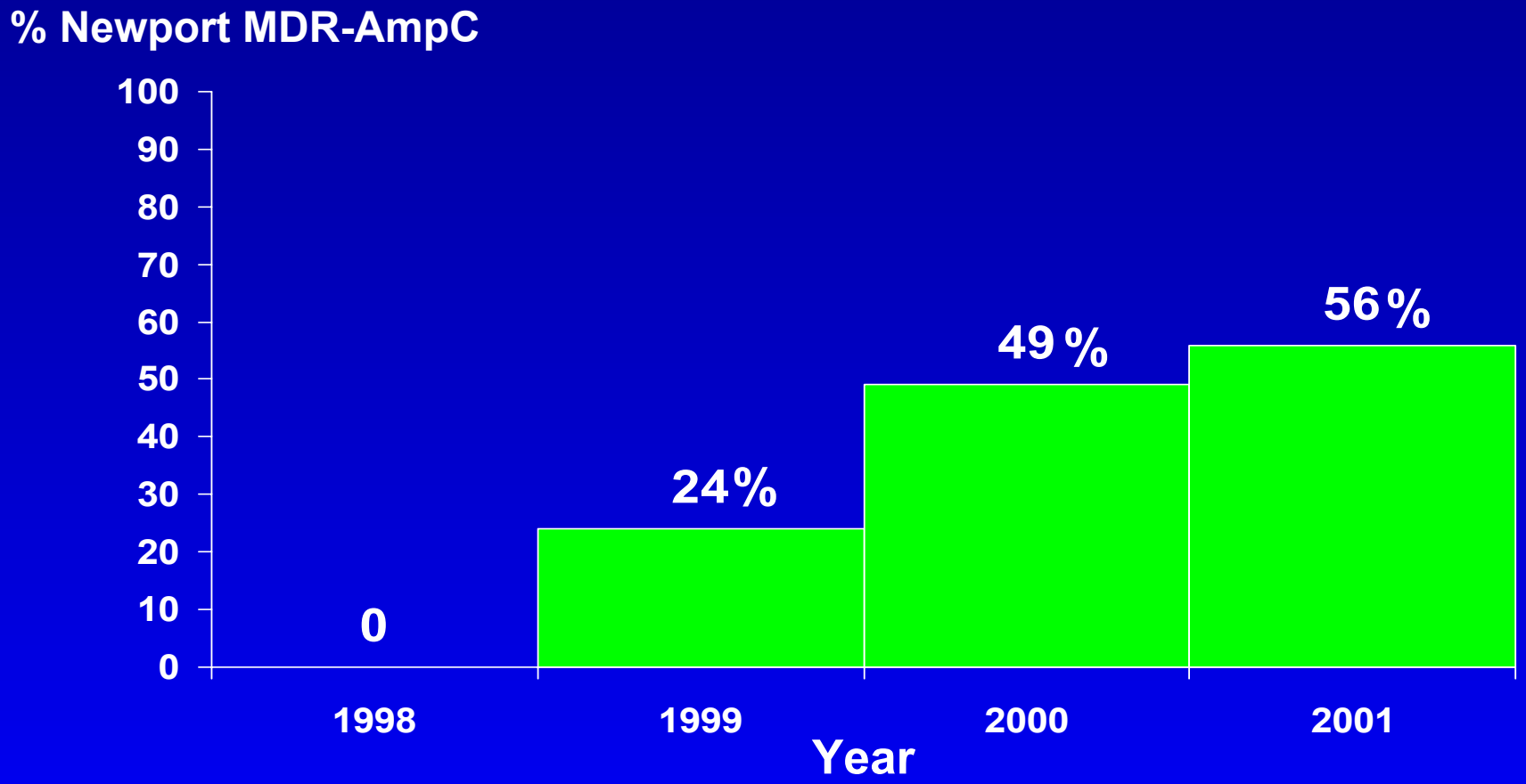
Sporadic Newport MDR-AmpC infections, Massachusetts

- Nov 2000: MA State lab noted 4 Newport MDR-AmpC isolates
  - 2 from ill dairy cows
  - 2 from ill persons --- one from a child who attended a daycare on another dairy farm

Investigation of Newport MDR-AmpC, Massachusetts, 1998-2001

- Determined antimicrobial resistance of all recent human *S.* Newport isolates
- Determined risk factors for human illness via a retrospective case-control study
- Obtained and tested isolates from dairy cattle

Proportion of Human *S.* Newport Isolates that were Newport MDR-AmpC, Massachusetts, 1998 – 2001



Massachusetts Department of Public Health

Characteristics of Patients with Newport MDR-AmpC Massachusetts, 1999-2001

- Compared with persons with susceptible *S.* Newport infection
  - More likely had bloody diarrhea
  - Less likely had international travel

Risk Factors for Human Newport MDR-AmpC Infection, Massachusetts, 1999-2001

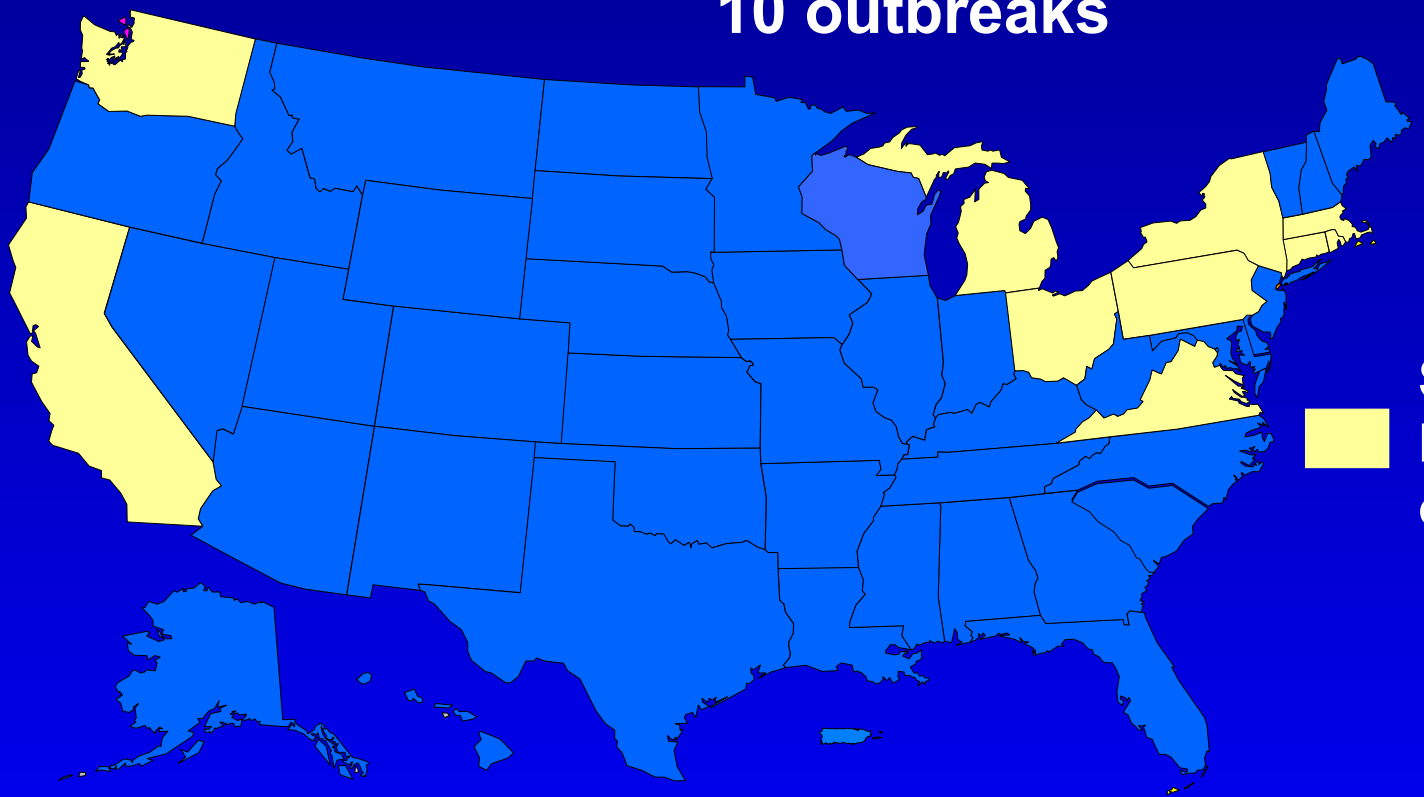
- Compared with well persons
  - More likely took an antibiotic in the past week
  - More likely had dairy farm exposure
  - Less likely ate yogurt

Review of cattle isolates Massachusetts and Vermont 2000-2001

- Detected *S.* Newport MDR-AmpC in stools of ill and well dairy cattle
- Many strains had same PFGE pattern as human isolates
- Dairy farms with Newport MDR-AmpC often had illness and deaths in cows
- On one farm, ill persons and milking cows had same strain

Outbreaks of Newport MDR-AmpC, 1999-2002

10 outbreaks



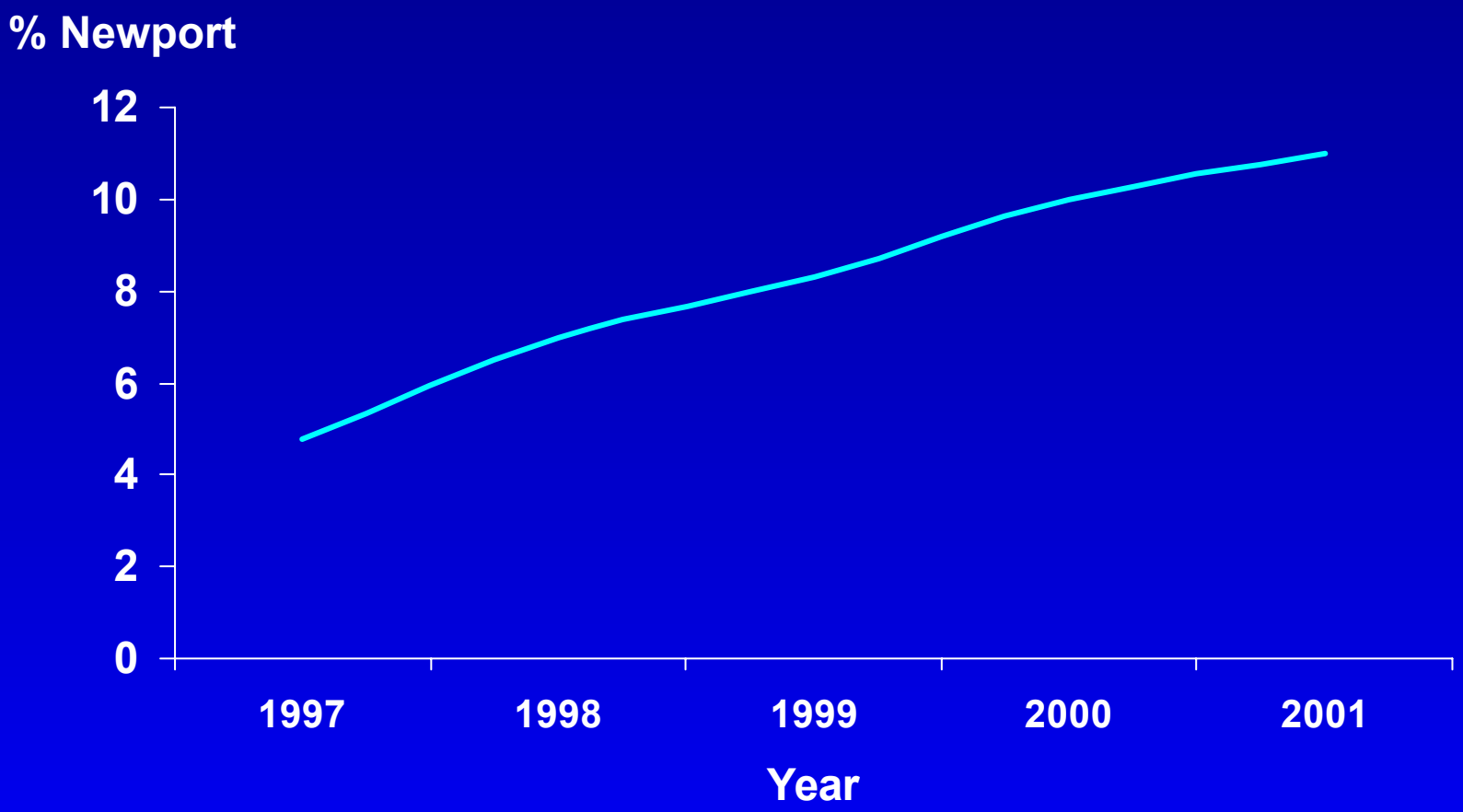
State with Newport MDR-AmpC outbreak

Based on reporting to CDC

Food Vehicles in Newport MDR-AmpC Outbreaks

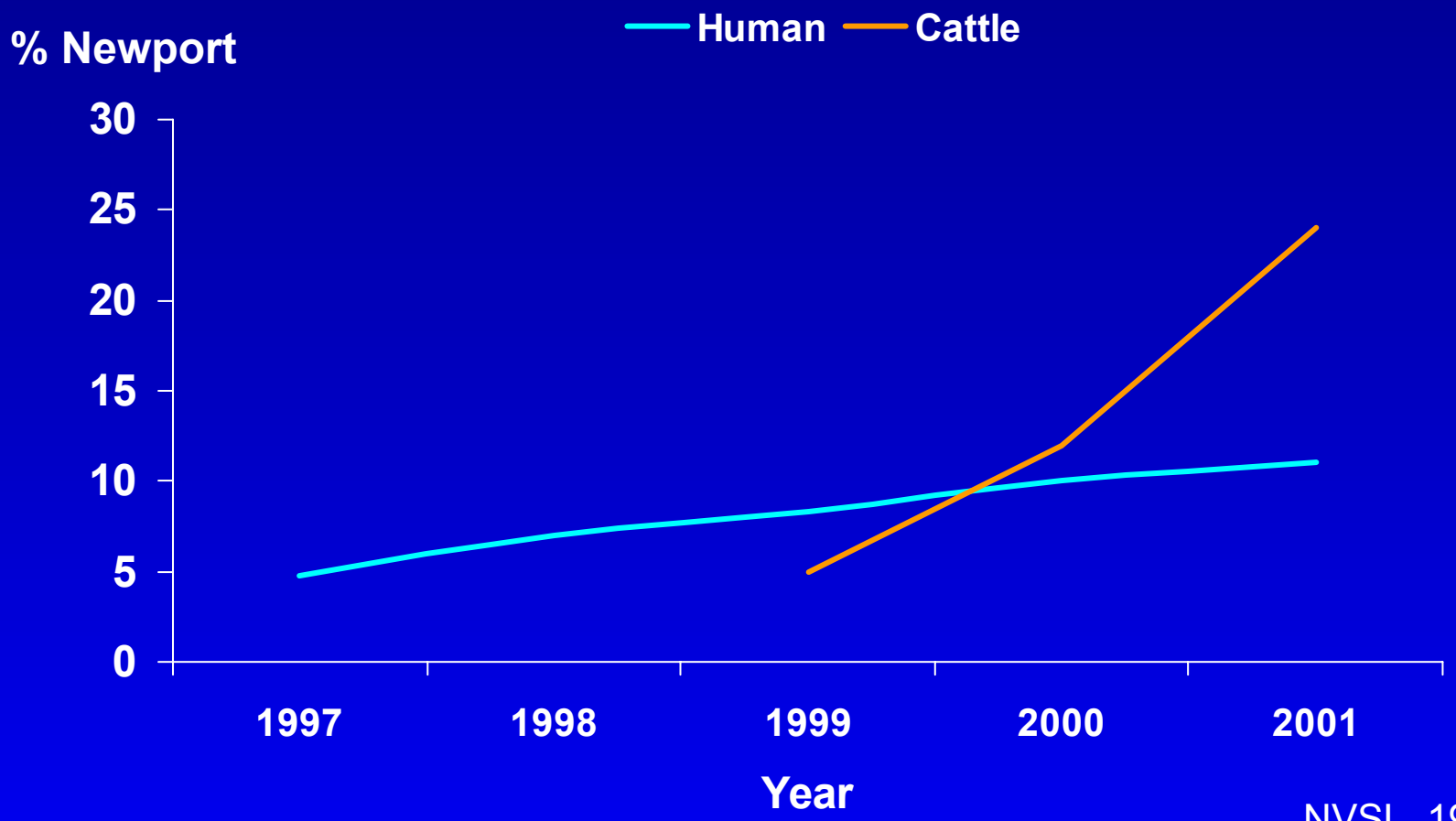
- Unpasteurized cheese/cream (3 outbreaks)
- Ground beef (2)
- Grape tomatoes (1)
- Turkey (1)
- Cilantro (1)
- Dish containing goat's blood (1)

Proportion of *Salmonella* that were *S.* Newport, Humans



CDC PHLIS, 1997-2001

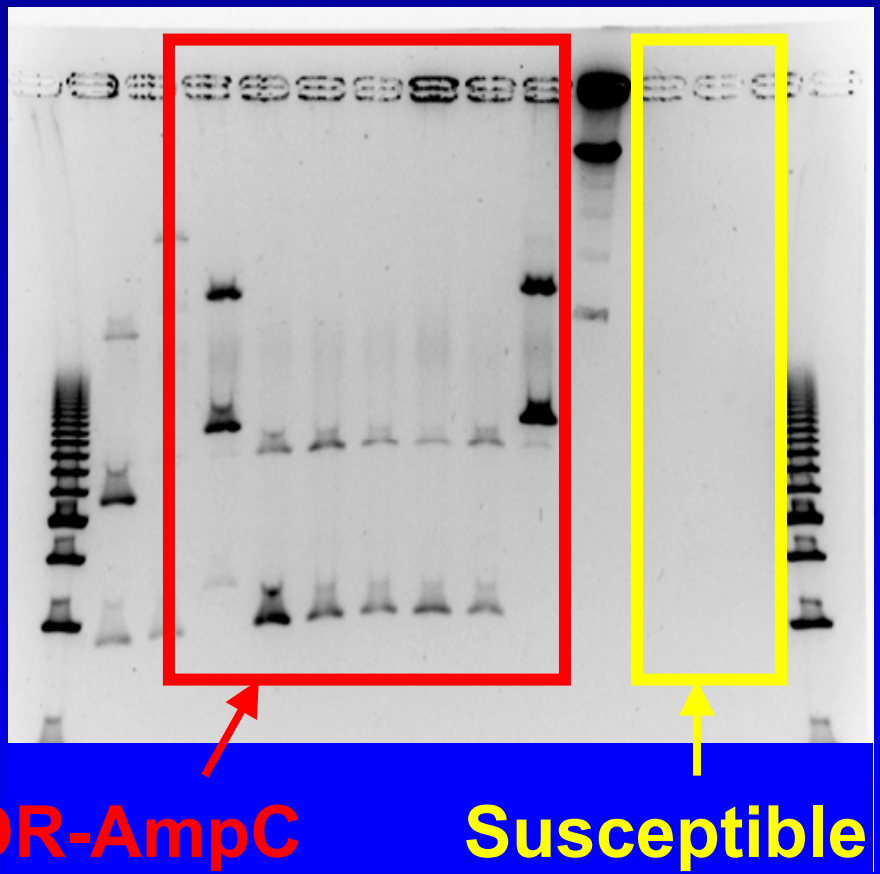
Proportion of *Salmonella* that were *S.* Newport, Humans and ill Cattle



NVSL, 1999-2001
CDC PHLIS, 1997-2001

Molecular Characterization of Newport MDR-AmpC

- Resistance is on transferrable plasmids
- Contains a *bla*$_{CMY}$ gene
  - •ampicillin
  - •amoxicillin/clavulanate (pcn-inhibitor)
  - •cefoxitin (cephamycin)
  - •ceftiofur, ceftriaxone (extended- spectrum cephalosporins)



Comparison of *S.* Typhimurium DT104 with Newport MDR-AmpC

S. Typhimurium DT104

- Illness in cattle
- Illness in persons in contact with cattle
- Bovine food vehicles (cheese, ground beef)
- ACSSuT
- Resistance genes on chromosome
- Epidemic in Europe

Newport MDR-AmpC

- Illness in cattle
- Illness in persons in contact with cattle
- Bovine food vehicles (cheese, ground beef)
- ACSSuT plus
- Resistance genes on plasmid
- Appears confined to U.S.

Summary

- The incidence of *S*. Newport human illness increased markedly in the late 1990s
- The increase in human *S.* Newport illness has been driven by an increase in a highly resistant strain, “Newport MDR-AmpC”
- Illness due to Newport MDR-AmpC is also emerging in cattle
- Risk factors for human illness include contact with cattle and consumption of bovine products (e.g., ground beef, unpasteurized cheese)

Summary (continued)

- There are similarities and differences between epidemic Newport MDR-AmpC and S. Typhimurium DT104
- Resistance is mediated by transferrable plasmids

CDC Activities

- Continuing surveillance through NARMS
- Investigating molecular mechanisms for resistance
- Conducting a case-control study of risk factors -- began April 2002 in FoodNet sites
- Publishing a CSTE letter and MMWR this month
- Assisting in outbreak investigations
- Encouraging studies of factors leading to emergence

Recommendations

- Investigate human clusters of *S.* Newport infections
  - Inform CDC of clusters rapidly, send 3 isolates for antibiotic resistance testing
  - Screen for MDR-AmpC using chloramphenicol
- Alert public health veterinarian or dept of agriculture
  - Suggest review of veterinary *Salmonella* isolates
  - Suggest investigation of animal clusters of *S.* Newport
  - Alert farm personnel about risk of human illness

Recommendations (continued)

- Alert clinical community because standard therapy for *Salmonella* may fail
- Determine whether raw milk or cheese made from it is sold in your state
  - Educate people, especially Hispanic community, about importance of pasteurization

Acknowledgements

- CDC
  - A. Gupta
  - C. Crowe
  - F. Angulo
  - M. Hoekstra
  - J. Whichard
  - S. Van Duyne
  - R. Tauxe
  - T. Barrett
  - M. Huddle
  - J. McClellan
  - S. Rossiter
- NARMS sites
- Massachusetts Department of Public Health
  - J. Fontana
  - A. Stout
  - B. Bolstorff
  - M. McGuill
  - B. Matyas
- Vermont Department of Health
  - S. Schoenfeld
  - B. Johnson
  - N. Pugsley

Selected abstracts on *S.* Newport

IDSA 2001: Gupta, A et al.

Multistate Investigation of Multidrug-Resistant *Salmonella* Serotype Newport In the Northeastern US, 2000: Human Infections associated with Dairy Farms

ICEID 2002: Fontana, J et al.

The Use of Pulsed Field Gel Electrophoresis and Automated Ribotyping to Monitor the Increased Prevalence of a Multidrug-Resistant *Salmonella* Serotype Newport in Massachusetts Associated with Cows

ICAAC 2001: Angulo, F et al.

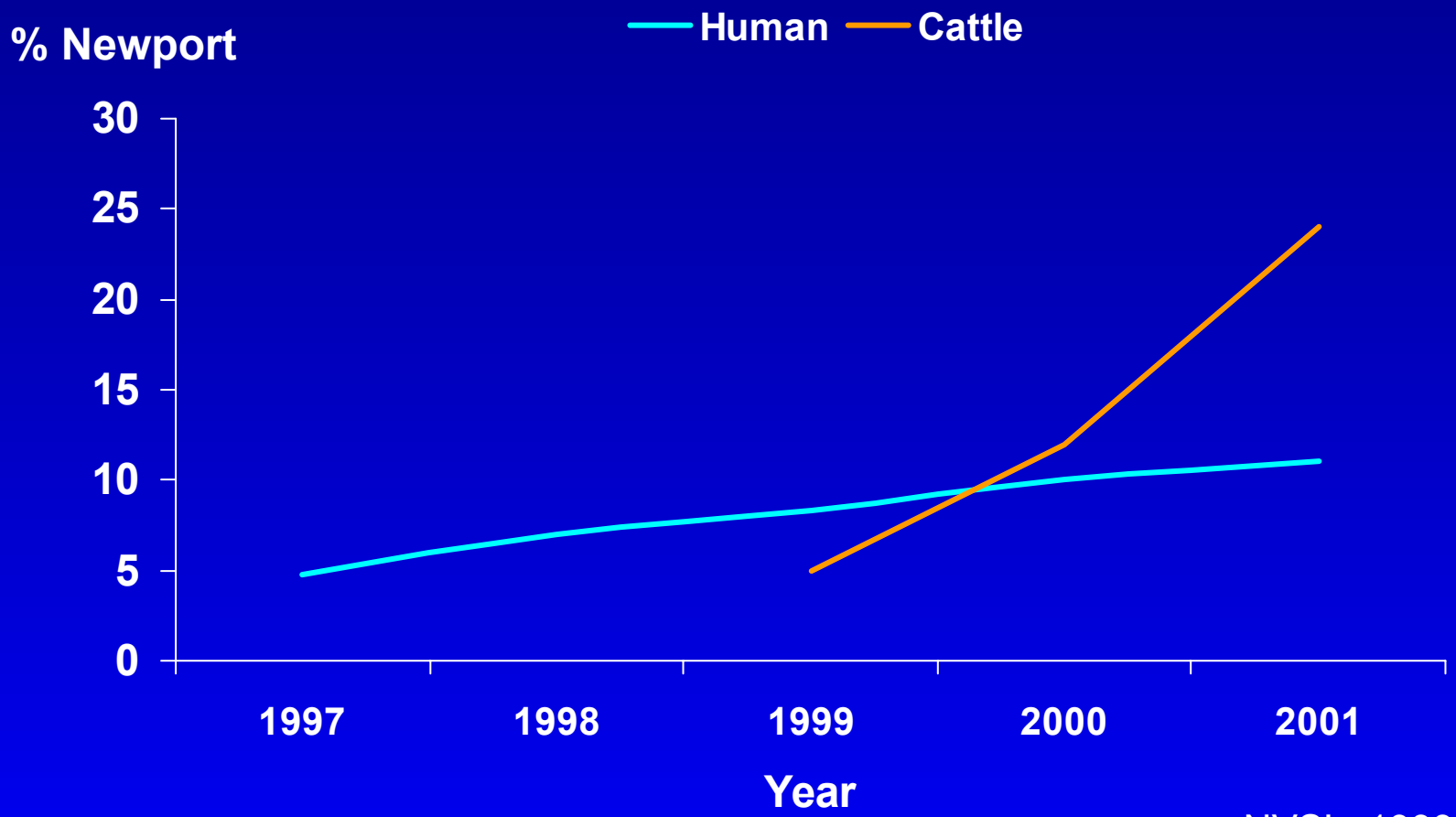
Three Prevalent Mulitdrug-Resistant Strains Among Human *Salmonella* Isolates in the US, 1999-2000: *S.* Typhimurium R-type ACSSuT, *S.* Typhimurium R-type AKSSuT, and *S.* Newport R-type ACSSuT

ICEID 2000: Joyce, K et al.

Emergence of a Multidrug-Resistant Strain of *Salmonella* Serotype Newport in the US: NARMS 1997-1999

www.cdc.gov/NARMS

Proportion of *Salmonella* that were Newport, Humans and ill Cattle

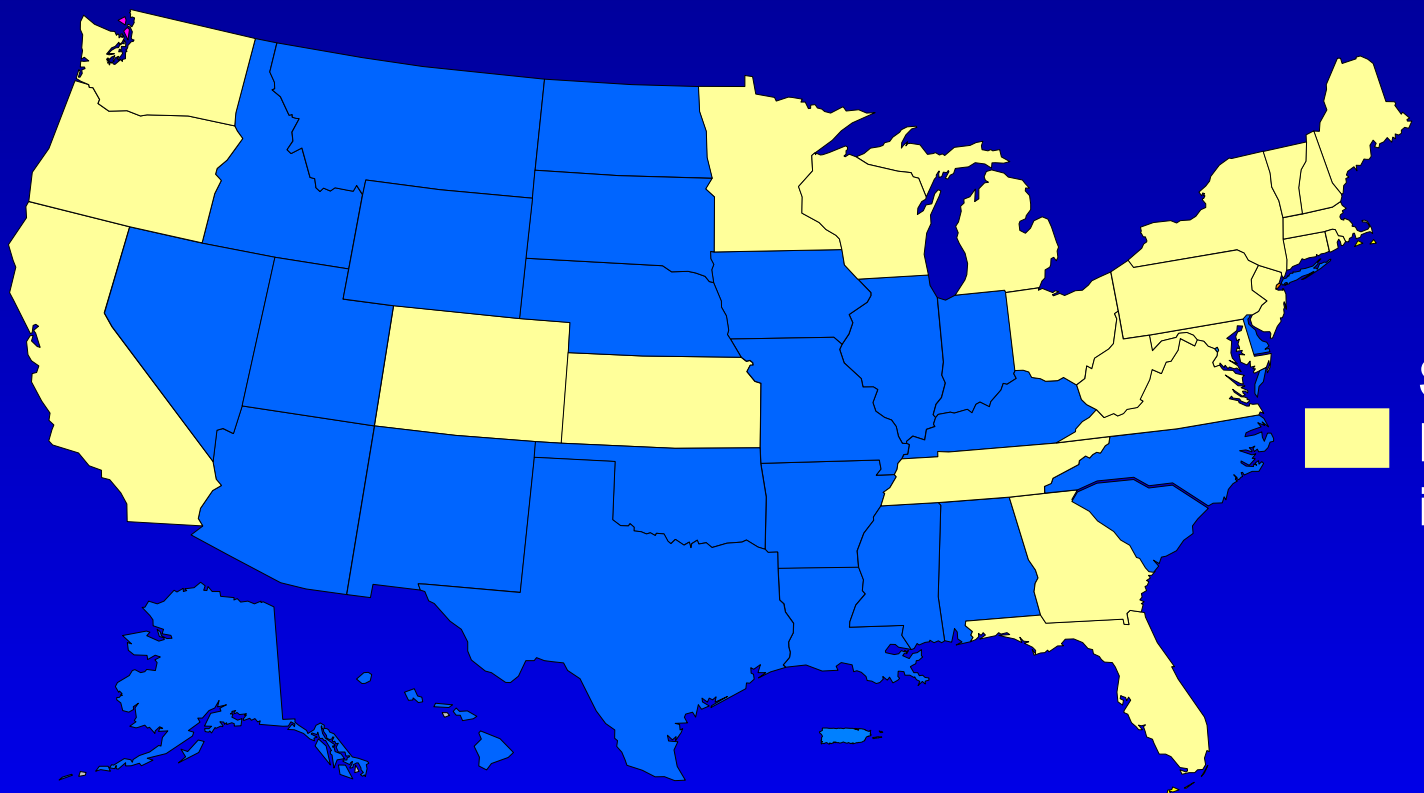


NVSL, 1999-2001
CDC PHLIS, 1997-2001

Additional resistance of Newport MDR-AmpC

- Of 78 Newport MDR-AmpC strains examined
  - 10% resistant to trimethoprim-sulfa
  - 6% resistant to gentamicin
  - 17% resistant to kanamycin

States reporting isolation of Newport MDR-AmpC, 1999-2002



State with Newport MDR-AmpC isolate

Based on reporting to CDC via NARMS or testing performed at state PHL